

Notice of Allowability

Application No.

10/085,774

Examiner

Jeanine A. Goldberg

Applicant(s)

SYLVAN, ANNA

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to June 13, 2005.
2. ☒ The allowed claim(s) is/are 1, 5-15, 17, 21-23.
3. ☒ The drawings filed on 27 February 2002 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____


JEANINE A. GOLDBERG
PRIMARY EXAMINER

DETAILED ACTION

1. This action is in response to the papers filed June 13, 2005. Currently, claims 1, 5-15, 17, 21-23 are pending.

REASONS FOR ALLOWANCE

2. The following is an examiner's statement of reasons for allowance.

Claim 1 is drawn to a method of determining the frequency of an allele in a population of nucleic acids by pooling nucleic acids from a population, performing primer extension and detecting the release of pyrophosphate. Claim 17 is drawn to a method of determining the amount of an allele in a sample by performing primer extension and detecting the release of pyrophosphate.

The declaration under 37 CFR 1.132 filed June 13, 2005 is sufficient to overcome the rejection of Newly amended Claims 1, 5-15, 17, 21-23. The declaration filed by Nyren, the sole inventor of WO 98/28440, states "Although I have worked extensively in the field of Pyrosequencing, it did not occur to me that Pyrosequencing could be used on pooled samples, for example to detect or analyse single nucleotide polymorphisms (SNPs) in pooled samples or for any form of allele quantification study" (page 2, point 5 of Declaration). Further, Nyren states "It would not have been obvious to a person skilled in the art that the Pyrosequencing method would have been sufficiently quantitative or accurate to be used in allele frequency determinations or in pooled samples" (page 4, point 8 of Declaration). Finally, Nyren states that "It was surprising that the Pyrosequencing method worked as well as it did on a quantitative level. It was

unforeseen that the Pyrosequencing approach would provide sufficiently quantitative data that would correlate sufficiently well to the allele frequencies to enable allele discrimination and quantification" (page 4, point 9 of Declaration).

In view the declaration, the combination of Suber in view of Nyren would not have been obvious at the time the invention was made for the reasons set forth by Pal Nyren.

3. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kambara et al (US 6,750,018, filed September 5, 2001) teaches "The photo-emission intensity observed upon hybridization with the mutant sequence shown in Table is the background light derived from impurities and pyrophosphate produced by decomposition of nucleotide substrates (dNTPs), and becomes zero by background adjustment. It is important to know the ratio of the wild type and mutant in a genome mixed samples or the like, which contain both the wild type and mutant sequences. In particular, in order to study relationship between diseases and SNPs, it is important to compare the incidence of SNPs of interest in genomes of patients and in healthy subjects. For that, it is necessary to analyze SNPs in an extremely large number of samples. A huge number of data have to be obtained since SNPs are numerous. In such a case, a correlation with a certain disease can be efficiently examined by measuring SNPs in pooled genomes of patients and pooled genomes of healthy subjects. Generally, the significance level for the incidence of SNPs is considered to

be more than 1% and the significance level for the correlation with disease is considered to be more than 5%. Therefore, in a mixed genome sample, the ratio of the incidence of SNPs has to be measured at the accuracy level of about 1%, which has been difficult using conventional methods. According to a method of the present invention, the ratio of the incidence can be determined at the accuracy level of about 1% by measuring the ratio of respective complementary strand extensions using two primers. FIG. 3(c) shows the result of the experiment discussed above. Namely, FIG. 3(c) shows results of measurement for a mixed genome sample containing both the wild type and mutant, according to the present invention" (col. 10).

4. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

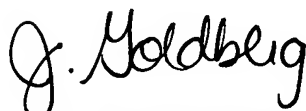
5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Art Unit: 1634

The Central Fax Number for official correspondence is (571) 273-8300.

A handwritten signature in black ink, appearing to read "J. Goldberg". The signature is fluid and cursive, with the first letter "J" being particularly large and stylized.

Jeanine Goldberg

Primary Examiner

August 15, 2005